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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/527,975	03/15/2005	Helene Le Buannec	0510-1230	7511

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EXAMINER	
WOODWARD, CHERIE MICHELLE	
ART UNIT	PAPER NUMBER
1647	

NOTIFICATION DATE	DELIVERY MODE
08/18/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

DocketingDept@young-thompson.com

Office Action Summary	Application No.	Applicant(s)	
	10/527,975	LE BUANNEC ET AL.	
	Examiner	Art Unit	
	CHERIE M. WOODWARD	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 May 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 21-28* is/are pending in the application.

4a) Of the above claim(s) *26-28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 21-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Formal Matters

1. Applicant's Response and Amendments filed 5/28/2010 are acknowledged and entered. Claims 4-20 and 29 have been cancelled by Applicant. Claims 1-3 and 21-28 are pending. Claims 26-28 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a non-elected inventions, there being no allowable generic or linking claim. Claims 1-3 and 21-25 are under examination.

Response to Arguments

Correction of Inventorship

2. Applicant provides copies of the PCT/IB/306 forms regarding co-inventors Peltre and Cohen. However, as previously stated of record, Applicant has not complied with 37 CFR 1.497(d) and (f). Applicant has not filed the statement from each person being deleted as required by 37 CFR 1.497(d). This requirement must be fulfilled regardless of Applicant's submission of the PCT/IB/306 documents. As stated of record and as plainly stated in 37 CFR 1.497(d), for a change of inventorship in a nonprovisional application filed under 35 USC 371:

If the oath or declaration filed pursuant to 35 U.S.C. 371(c)(4) and this section names an inventive entity different from the inventive entity set forth in the international application, or if a change to the inventive entity has been effected under PCT Rule 92 bis subsequent to the execution of any oath or declaration which was filed in the application under PCT Rule 4.17(iv) or this section and the inventive entity thus changed is different from the inventive entity identified in any such oath or declaration, applicant **must submit**:

(1) A statement from each person being added as an inventor and from each person being deleted as an inventor that any error in inventorship in the international application occurred without deceptive intention on his or her part;

(2) The processing fee set forth in § 1.17(i); and

(3) If an assignment has been executed by any of the original named inventors, the written consent of the assignee (see § 3.73(b) of this chapter); and

(4) Any new oath or declaration required by paragraph (f) of this section.

Advisory Notice

3. The examiner does not decide matters related to entrance of Powers of Attorney in cases. This is under the purview of the Office of Data Management. The file wrapper shows that the new Power of Attorney was accepted on 9/18/2009 and that the address and customer number was been changed effective 9/22/2009. See PAIR.

4. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

5. Applicant is requested to thoroughly check the specification for errors and make appropriate corrections (see, i.e., p. 64 where a sequence is missing a SEQ ID NO). Applicant was previously advised of record to check the specification for errors.

Objections/Rejections Maintained

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1-3 and 21-25 remain rejected under 35 U.S.C. 102(b) as being anticipated by Zagury et al., (WO 02/011759 A1, published 2 February 2002, in French, he certified English translation of which found in US 2004/0028647 A1, the US patent application filing under 35 USC 371 PCT/FR01/02575), for the reasons of record and the reasons set forth herein.

Applicant argues that Zagury fails to suggest the composition comprising more than 1% and less than 40% of the TNFα protein molecules covalently linked to the KLH and more than 60% of the TNFα molecules non-covalently associated with the KLH (Remarks, pp. 7 and 11-12). Applicant argues that the method of preparation taught by Zagury results in a composition in which "essentially 100%" of the "biological factor" is covalently linked to the KLH (Remarks, p. 8). Applicant argues that the previously

submitted Declaration provides experimental evidence demonstrating that the presently claimed product is distinguishable from that in the Zagury reference (Remarks, pp. 9-10). Applicant argues that the Office Action discounts Declarant's statements and data in Exhibit B (Remarks, p. 10).

Applicant's arguments have been fully considered, but they are not persuasive. Regarding Applicant's arguments that the Office Action discounted Declarant's statements and the data in Exhibit B, Applicant is mistaken. The examiner full considered the statements and the data, but found them unpersuasive.

The examine hasr revisited Applicant's Declaration and Figures. The examiner notes that the ratios of KLH:TNFα in Figures 1 and 2 of the Declaration differ in such a way that the composition of Zagury could be distinct from the instantly claimed composition, but any such distinction is not to be found based on the instant claims as written.

In the Declaration, Figure 1 represents the method of preparing the instant product according to example 9 of the instant application and Figure 2 represents the method of preparing a KLH:TNFα conjugate according to Zagury et al. Solely using the exemplary Figure 1 in the Declaration, the ratio of 1:50 (KLH:CK) would result in a variety of KLH:CK conjugate configurations, including one in which multiple TNFα molecules could be daisy-chained (polymerized) off of one KLH molecule. It could also result in a configuration in which one KLH molecule would contain multiple TNFα molecules. The high ratio of cytokine to KLH would result in competitive binding to the KLH. Similarly, solely using the exemplary Figure 2 in the Declaration, the ratio of 5:1 KLH:CK could result in TNFα having double or single bonds to the KLH and it could also result in a configuration of multiple KLH molecules linked to one another in a daisy-chain format with only one or two molecules of TNFα linked to one of the KLH molecules.

Neither of these Figures are not dispositive of the question of percent of covalent bonding in either the instant composition or that of the prior art Zagury reference. Depending on the structure of the conjugates in Figures 1 and Figure 2 of the Declaration, there may be more or less covalent bonding from one configuration than another, if one is to view (define) "covalent bonding" as the bond between KLH and TNFα. If multiple KLH are daisy-chained together, with few cytokines present (because of, for example, the KLH:cytokine ratios) then there would be fewer covalent bonds between the TNFα and the KLH because of the molecular polymerization (daisy-chaining). KLH is a huge molecule, compared to even multimers of TNFα. Ratios between the amount of each protein, as well as incubation time with the cross-linking/bonding agent, and amount of cross-linking/bonding agent (i.e. gluteraldehyde) would also need to be taken into consideration. Both gluteraldehyde and formaldehyde bind primary amines and also

secondary amines on lysines. One would also need to take into account whether the gluteraldehyde was freshly prepared or if it was purchased commercially because commercially purchased gluteraldehyde tends to polymerize and you get differences in fixation and cross-linking. None of these limitations are present in the instant claims such that the claims would provide a sufficient basis to distinguish the physical characteristics of the composition of conjugates from that of the prior art.

The instant claims under examination are composition claims. The examiner suggests that Applicant consider product-by-process claim limitations (provided there is sufficient support in the instant specification for such claim limitations and that the addition of such limitations would not result in new matter) for the instant claims. Although the examiner is still required to examine the claims based on the product in a product-by-process claims, in the instant situation process limitations would provide a basis to more clearly distinguish the instantly claimed composition from that in the prior art in such a way that one would be apprised of the ratio of KLH:cytokine, the amount of cross-lining/bonding agent used, and the incubation time required to produce a composition in which 60% or more of the bonds are non-covalent bonds. These additional product-by-process limitations would reasonably be known and understood to affect the physical properties of the composition in such a way as to distinguish it from the composition of the prior art because of the likelihood that it would result in a physically distinct composition.

Applicant is encouraged to review Example 9 in the specification. However, the examiner notes that although this example is titled "Preparation of murine KLH-TNFα heterocomplex" the steps in line 16 recite the addition of IFNα. It may be that the recitation of IFNα in line 16 is a typographical error. If this is the case and the recitation is an obvious mistake, then appropriate correction is requested. Applicant's attention is also drawn to Example 32 (p. 63 of the specification).

The examiner has fully considered the Declaration and Figures of Applicant and the arguments of Applicant's Representaive. Based on the submissions and arguments, there is presently insufficient data to conclude that the instant invention is, in fact, different from that of the prior art. A very careful review of the prior art, the instant specification, the Declaration and Figures, and the arguments of Applicant's Representative do not provide sufficiently persuasive evidence or clear rationale for distinguishing the instantly claimed invention from that of the prior art.

Should Applicant wish to present further evidence in response to the instant rejection, the examiner will consider it after-final, if it directly responds to the instant rejections and suggestions to amend the claims in such a way as to advance and promote compact prosecution.

Provisional Obvious-Type Double Patenting Rejections

8. Claims 1-3 and 21-25 remain provisionally rejected on the ground of nonstatutory double patenting over claims 1-4, 6-8, 10-12, 14-17, and 19 of copending Application No. 11/735,319, for the reasons of record and the reasons set forth herein. The rejection over copending claims 2-4, 6-8, 10-12, 14-17, and 19 of the '319 application is moot in light of the cancellation of these co-pending claims.

Applicant requests that the instant rejection be held in abeyance. Applicant's request is denied. A request to hold a rejection in abeyance is not a proper response to a rejection. Rather, a request to hold a matter in abeyance may only be made in response to an objection or requirements as to form (see MPEP 714.02 and 37 CFR 1.111(b)). Applicant is specifically referred to CFR 1.111(b), which states that "[i]n order to be entitled to reconsideration or further examination, the applicant or patent owner must reply to the Office action. The reply by the applicant or patent owner must be reduced to a writing which distinctly and specifically points out the supposed errors in the examiner's action and must reply to every ground of objection and rejection in the prior Office action. The reply must present arguments pointing out the specific distinctions believed to render the claims, including any newly presented claims, patentable over any applied references. If the reply is with respect to an application, a request may be made that objections or requirements as to form not necessary to further consideration of the claims be held in abeyance until allowable subject matter is indicated. The applicant's or patent owner's reply must appear throughout to be a bona fide attempt to advance the application or the reexamination proceeding to final action. A general allegation that the claims define a patentable invention without specifically pointing out how the language of the claims patentably distinguishes them from the references does not comply with the requirements of this section.

Applicant's arguments that the instant claims are directed to heterocomplexes, whereas the claims of the '319 application are directed to inactivated TNFα (Remarks, pp. 13-14) are not persuasive. Claim 1 of the '319 application requires a composition comprising inactivated TNFα and an inactivated peptide fragment. As stated of record, the specification of the '319 application teaches immunogen-carrier conjugates comprising TNFα as the immunogen and KLH as the carrier at paragraphs 48, 53, 58, and Figure 2. The '319 application comprises the same KLH-immunogen conjugates as the instant application (compare specifications), where the conjugates comprise covalent bonds and are conjugated using glutaraldeyhde (see Preparation 10, paragraphs 140-148 of the '319 application). Absent evidence to the contrary, the KLH conjugates of the '319 application are heterocomplexes.

Applicant is reminded that MPEP § 804 (II) states, "When considering whether the invention defined in a claim of an application would have been an obvious variation of the invention defined in the

claim of a patent, the disclosure of the patent may not be used as prior art. *General Foods Corp. v. Studiengesellschaft Kohle mbH*, 972 F.2d 1272, 1279, 23 USPQ2d 1839, 1846 (Fed. Cir. 1992). This does not mean that one is precluded from all use of the patent disclosure." (Emphasis added). "Further, those portions of the specification which provide support for the patent claims may also be examined and considered when addressing the issue of whether a claim in the application defines an obvious variation of an invention claimed in the patent. *In re Vogel*, 422 F.2d 438, 441-42, 164 USPQ 619, 622 (CCPA 1970)." Applicant is also referred to *In re Basell Poliolefine Italia*, 547 F.3d 1371 (Fed. Cir. 2008).

Accordingly, the provisional rejection is maintained.

Conclusion

NO CLAIM IS ALLOWED.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CHERIE M. WOODWARD whose telephone number is (571)272-3329. The examiner can normally be reached on Monday - Friday 9:30am-6:00pm (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol can be reached on (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Cherie M. Woodward/
Primary Examiner, Art Unit 1647